Response to Amendment

The amendment filed 4/11/11 has been entered into the record. Claims 1-52, 59-70 and 74-85 have been cancelled. Claims 53-58,88,90-94 has been amended. Claim 95 has been added. Claims 53-58, 71-73, 86-95 are pending and are under examination.

Specification

The amendment to the specification is acknowledged.

Election/Restriction

Applicants' requests for rejoinder of the species SEQ ID NO:22 and 23 is acknowledged. However, it is noted that species SEQ ID NO: 22-23 have been cancelled in the claims. Please amend the claims to recite these species so that they can be considered.

Claim Rejections Withdrawn

The rejection of claims 53-58, 71-73 and 86-94 under 35 U.S.C. 112, first paragraph, (scope of enablement) is withdrawn in view of the amendment to the claims.

The rejection of claims 53-58, 71-72, 86, and 88-94 under 35 U.S.C. 102(b) as being rejected by Wright. US 5,730,989 (3/24/98) as evidenced by Hideo et al (JP20023550742A2, cited in IDS) is withdrawn in view of the amendment to the claims..

The rejection of claims 53-55, 71-72, 86 and 90 under 35 U.S.C. 102(b) as being rejected by Hideo et al (JP20023550742A2, cited in IDS) as evidenced by Wright et al US 5,730,989 (3/24/98) is withdrawn in view of the amendment to the claims. Applicant's arguments are considered but are moot in view of the withdrawal of the rejection.

The rejection of claims 53-58, 71-72, 86 and 90-94 under 35 U.S.C. 103(a) as being unpatentable over Hideo et al (JP20023550742A2, cited in IDS) in view of Wright et al US 5,730,989 (3/24/98) is withdrawn in view of the amendment to the claims. Applicants' arguments are considered but are moot in view of the withdrawal of the rejection.

The rejection of claims 53-55, 71-72, 86, 88-89 and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hideo et al (JP20023550742A2, cited in IDS) as evidenced by Wright et al in view of Finlay et al. WO 02/053181, cited in IDS is withdrawn in view of the

amendment to the claims. Applicants' arguments are considered but are moot in view of the withdrawal of the rejection.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 53-58, 71-73 and 86-95 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained. **This is a written description rejection.**

Claim 53 is drawn to a method for eliciting an immune response against an A/E pathogen, or component thereof, in a ruminant comprising administering to the ruminant an effective amount of a composition comprising:

i) an isolated polypeptide which comprises an amino acid sequence having at least 75% sequence identity to the sequence of SEQ ID NOs: 24 or an immunogenic fragment or variant thereof, or

a cell culture supernatant which comprises an isolated polypeptide comprising an amino acid having at least 75% sequence identity to the sequence of SEQ ID NOs: 24 or an immunogenic fragment or variant thereof, thereby eliciting an immune response in the ruminant.

Claim 54 is drawn to a method for reducing colonization of an A/E pathogen in an ruminant, the method comprising administering to the ruminant an effective amount of a composition comprising:

i) an isolated polypeptide which comprises an amino acid having at least 75% sequence identity to the sequence of SEQ ID NOs: 24 or an immunogenic fragment or variant thereof or

(ii) a cell culture supernatant which comprises a polypeptide comprising an amino acid having at least 75% sequence identity to the sequence of SEQ ID NOs: 24 or an immunogenic fragment or variant thereof, thereby reducing colonization of the A/E pathogen in the ruminant

Claim 55 is drawn to a method for reducing shedding of an A/E pathogen in a ruminant comprising administering to the animal an effective amount of a composition comprising:
i) an isolated polypeptide which comprises an amino acid having at least 75% sequence identity to the sequence of SEQ ID NOs: 24 or an immunogenic fragment or variant thereof,
or ii) a cell culture supernatant which comprises a polypeptide comprising an amino acid having at least 75% sequence identity to the sequence of SEQ ID NOs: 24 or an immunogenic fragment or variant thereof, thereby reducing shedding of the A/E pathogen in the animal.

The claims are drawn to a large genus of variants of proteins comprising at least 75% sequence identity to SEQ ID NO: 24 comprising species that are substitution, deletion and/or insertion variants of SEQ ID NO: 24 and immunogenic fragments or variants of a polypeptide comprising an amino acid sequence having at least 75% sequence identity to SEQ ID NO: 24 The scope of the claims encompasses numerous structural species resulting in a highly variant genus composed of members with a significant number of structural differences. Up to 25% of the sequence of SEQ ID NO: 24 or fragments or variants thereof or fragments or variants thereof of a polypeptide comprising an amino acid sequence having at least 75% sequence identity to SEQ ID NO: 24 can be substituted, deleted and/or inserted.

The claim requires that these genus of variants have the property of stimulating an immune response against any A/E pathogen infection in a ruminant and reducing colonization or shedding of any A/E pathogen.

p. 18 of the specification defines an "immune response" as follows:

An "immune response" includes, but is not limited to, one or more of the following responses in a mammal: induction of antibodies, B cells, T cells (including helper T cells, suppressor T cells, cytotoxic T cells, γδ T cells) directed specifically to the antigen(s) in a composition or vaccine, following administration of the composition or vaccine. An immune response to a composition or vaccine thus generally includes the development in the host mammal of a cellular and/or antibody- mediated response to the composition or vaccine of interest. In general, the immune response will result in prevention or reduction of infection by an A/E pathogen; resistance of the intestine to colonization by the A/E pathogen; or reduction in shedding of the A/E pathogen.

The specification describes an actual reduction to practice of SEQ ID NO: 24 but does not reduce to practice fragments or variants of a polypeptide having an amino acid sequence having at least 75% sequence identity to SEQ ID NO: 24 that induce an immune response (induction of antibodies, B cells, or T cells including
helper T cells, suppressor T cells, cytotoxic T cells, y5 T cells see definition of immune response above) that results in reduction or prevention of infection by an A/E pathogen; resistance of the intestine to colonization by the A/E pathogen; or reduction in shedding of the A/E pathogen.

The specification does not describe the common structure of the genus to which the claims are drawn that correlates with the property of stimulating an immune response (as defined in the specification) against any A/E pathogen (including treating or preventing) infection in an animal and reducing colonization or shedding of any A/E pathogen.

There are no sufficient identifying characteristics of immunogenic fragments or variants of any polypeptide (including SEQ ID NO: 22-24) having an amino acid sequence having at least 75% sequence identity to SEQ ID NO: 24; there are also no sufficient identifying characteristics of proteins that are 75% identical to SEQ ID NO: 2; these variants are described only by a functional characteristic (stimulating an immune response (see definition of immune response above) against any A/E pathogen including treating or preventing infection in ruminant and reducing colonization or shedding of any A/E pathogen), without any known or disclosed correlation between the biological function and structural characteristics. *In re Bell* F.2d 781, 26 USPQ2d (Fed. Cir 1993).

It is unpredictable from the disclosure of SEQ ID NO: 24 (NleA of enterohemorrhagic E. coli (EPEC) and SEQ ID NO: 22-23 (NleA from C. rodentium and Enteropathogenic E. coli) which have 83% and 89.5 % sequence identity respectively to SEQ ID NO: 24 which members of the large and variant genus will stimulate an immune response against any A/E pathogen (including treating or preventing) infection in animal and reducing colonization or shedding of any A/E pathogen. The description of proteins that are 83% or 89.5% identical to SEQ ID NO: 24 does not provide a representative number of species of proteins that are at least 75% identical to SEQ ID NO: 24 and that performs the functions claimed.

Colman et al (Research in Immunology 145: 33-36, 1994, p.33 column 2, p. 35 column 1) disclose that single amino acid changes in an antigen can effectively abolish the interaction

with an antibody entirely and that a very conservative amino acid substitution may abolish antibody binding and a non-conservative amino substitution may have little effect in antibody binding. Houghten et al. (New Approaches to Immunization, Vaccines 86, Cold Spring Harbor Laboratory, p. 21-25, 1986) taught the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten et al state (see page 24): "One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool."

Even though one could screen for proteins that are 75%, 76%, 77% etc identical to SEQ ID NO: 24 or immunogenic fragments of variants of SEQ ID NO: 24 and immunogenic fragments and variants of proteins that comprise an amino acid sequence having at least 75% sequence identity) and that stimulate an immune response against any A/E pathogen (including treating or preventing) infection in animal and reducing colonization or shedding of any A/E pathogen, the courts have held that possession of a genus may not be shown by merely describing how to obtain members of the claimed genus or how to identify their common structural features. The written description requirement is separate and distinct from the enablement requirement (See also *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 920-23, 69 USPQ2d 1886, 1890-93 (Fed. Cir. 2004) and adequate written description requires more than a mere reference to a potential method for identifying candidate polypeptides. The purpose of the written description requirement is broader than to merely explain how to 'make and use' [the invention] *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1114 (Fed. Cir. 1991). In such an unpredictable art, as set forth supra, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See *Noelle v Lederman*. 355 F. 3d 1343, 1350, 69 USPQ2d 1508, 1514 (*Fed. Cir. 2004*) and *In re Alonso* (Fed. Cir. 2008-1079). In the instant case, no immunogenic fragment or variant of a protein that is at least 75% identical to SEQ ID NO: 24 and has the function of eliciting an immune response (see definition above), treating or preventing) infection in animal and reducing colonization or shedding of any A/E pathogen is disclosed. Similarly, a

representative number of proteins that are at least 75% identical 75 to SEQ ID NO: 24 and has the function of eliciting an immune response (see definition above), treating or preventing) infection in animal and reducing colonization or shedding of any A/E pathogen is not disclosed.

Therefore, Applicants as of the time of filing were not in possession of the full genus of immunogenic fragments and variants of a polypeptide at least 75% identical to SEQ ID NO: 24, and proteins which have at least 75% sequence identity to SEQ ID NO: 24 that have the function of eliciting an immune response (see definition above), treating or preventing) infection in animal and reducing colonization or shedding of any A/E pathogen. Applicants at the time of filing were only in possession of the SEQ ID NO: 22-23 which are 83% and 89.5 % identical to SEQ ID NO: 24, respectively, as well as in possession of SEQ ID NO: 24.

For Further guidance regarding compliance with the written description requirement, Applicants are directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001 and revision of the Written Description Training materials, Revision 1 March, 2008 http://www.USPTO.gov/web/menu/written.pdf.

Applicants' arguments and the response:

Applicants submit that the specification describes at least 3 variant of SEQ ID NO: 24, i.e. NleA polypeptides from enteropathogenic E. coli (EPEC), C. rodentium as well as enterohemorrhagic E. coli (EHEC) which fall within the presently claimed sequence identity and that immunogenic fragment clarifies that only fragments capable of eliciting an immune response are contemplated. Applicants' submission is considered but is unpersuasive. While, Applicants have described 2 polypeptides that comprise an amino acid sequence having 83% and 89.5 % sequence identity to SEQ ID NO: 24 i.e. SEQ ID NO: 22-23, Applicants at the time of filing were not in possession of the genus of proteins that are at least 75% identical to SEQ ID NO; 24 and the genus of immunogenic fragments or variants of proteins that are at least 75% identical to SEQ ID NO: 24 that have the function of eliciting an immune response (see definition above), treating or preventing) infection in animal and reducing colonization or shedding of any A/E pathogen, for the reasons set forth above in the rejection. The description of 2 proteins that are 83% and 89.5% identical is not a representative number of species of proteins that are 75% identical, for example, and immunogenic fragments and variants thereof that have the function of

eliciting an immune response (see definition above), treating or preventing) infection in animal and reducing colonization or shedding of any A/E pathogen.

As to Applicants submission that immunogenic fragment clarifies that only fragments capable of eliciting an immune response are contemplated, adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiefs v. Revel,* 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.,* 18 USPQ2d 1016. *Vas-Cath Inc. V. Mahurkar,* 19 USPQ2d 111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." In the instant case, a representative number of the genus of immunogenic fragments or variants of a protein having at least 75% sequence identity to SEQ ID NO: 24 and a representative number of the genus of proteins at least 75% identical to SEQ ID NO: 24 ***and*** that have the functions recited in the claims have not been described and thus applicants were not in possession of the genus of proteins required to practice the instant methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 53-58, 71-72 and 86-95 under 35 U.S.C. 102(b) as being rejected by Finlay et al. WO 02/053181 (cited in IDS) as evidenced by Hideo et al. (JP2002350742A2, cited in IDS, see partial translation attached as Appendix B) is maintained

Finlay et al teach a method for eliciting an immune response against an A/E pathogen or component thereof or a method for reducing colonization of an A/E pathogen or a method of reducing shedding (thus treating an infection by an A/E pathogen) in ruminant comprising administering to the ruminant an effective amount of a composition comprising a culture supernatant comprising a polypeptide which comprises an amino acid sequence substantially identical to SEQ ID NO: 24. See p. 37-39 claims 1-26. Said culture supernatant is prepared from *E. coli* EHEC O157:H7 under identical conditions as the instant specification (see example 1 and compare to preparation of cell culture supernatant to maximize the synthesis of cell culture supernatant proteins on p. 23 of Finlay et al) under which a protein comprising the sequence of SEQ ID NO: 24 or NleA (see annotation for SEQ ID NO: 24 in sequence listing) is produced. As evidenced by Hideo et al E. coli EHEC O157:H7 (see Appendix A disclosing a protein at least 75% identical to SEQ ID NO: 24) makes a protein comprising the sequence of SEQ ID NO: 24. Since Finlay et al teach a culture supernatant prepared from E. coli EHEC O157:H7 under identical conditions as in the instant composition, said culture supernatant is a composition or culture supernatant which comprises a polypeptide which comprises an amino acid sequence substantially identical to the sequence of SEQ ID NOs: 24 and inherently comprises 20% of the cell protein present in the composition. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Also, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in

fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency). See MPEP2112 (I and II).

Said animal is bovine or ovine. See p. 12 3rd full paragraph.

Said A/E pathogen is enterohemorrhagic E. coli 0157:H7 or E. coli 0157:NM. See p. 37 claims 2-3.

Said composition comprises pharmaceutically acceptable carrier (p. 18 last paragraph) and further comprises EspA, EspB, EspD, EspC, intimin and Tir (see p. 23 example 1 and figure 1 and p. 37claim 9). Said composition further comprises an adjuvant (see p. 19 and p. 37 claims 4-8).

Applicants' argument and the response:

Applicant argues that to support a rejection under 35 USC 102, a single prior art reference must describe each and every element either expressly or inherently of the rejected claims (MPEP section 2131). Applicants' arguments are considered but are not persuasive. This is because a 35 U.S.C. 102 rejection over multiple references has been held to be proper when the extra references are cited to show that a characteristic not disclosed in the reference is inherent. See MPEP 2131.

Applicants argue that the claims have been recited to recite the term "isolated which as defined in the specification refers to a compound that is "separated from the components that naturally accompany it" (see for example, p. 10 lines 20-21). Applicants argue that Finlay et al do not teach methods relating to an "isolated" polypeptide as claimed.

Applicants' arguments are carefully considered but are not persuasive. The methods of the instant claims are also drawn to administering a cell culture supernatant which comprises an isolated polypeptide comprising an amino acid sequence having at least 75% sequence identity to the sequence of SEQ ID NO: 24 , or an immunogenic fragment or variant thereof".

The definition of isolated on p. 10 lines 20-28 is set forth below:

A compound is "substantially pure" or "isolated" when it is separated from the components that naturally accompany it. Typically, a compound is substantially pure

when it is at least 10%, 20%, 30%, 40%, 50%, or 60%, or more generally at least 70%, 75%, 80%, 85%, 90%, 95%, or 99% by weight, of the total material in a sample. Thus, for example, a polypeptide that is chemically synthesized or produced by recombinant technology will be generally be substantially free from its naturally associated components. A polypeptide will also generally be substantially pure if it is separated from its naturally associated components by physical techniques, such as centrifugation, precipitation, column chromatography, gel electrophoresis, HPLC, etc.

The definition of isolated does not completely exclude additional components that naturally accompany it or other material e.g. 10% by weight of the total material in a sample. Furthermore, the recitation of cell culture supernatant in the claims encompasses material that naturally accompany the isolated polypeptide. Thus, the claims with regards to the cell culture supernatant does not exclude natural material as evidenced by the definition of cell culture supernatant in the specification on p. 9 lines 22-27:

A "cell culture supernatant," as used herein, refers generally to a supernatant derived from culturing a bacterium or other organism (e.g., yeast) or cell (e.g., insect cell) that is capable of secreting one or more of a polypeptide comprising an amino acid sequence substantially identical to the sequence of any one of SEQ ID NOs: 22- 43, 59, 73-84 or a fragment or variant thereof, or an immunogenic portion thereof, into the cell culture medium.

Finlay et al anticipates the instant the cell culture supernatant and the instantly claimed methods of use for the reasons set forth above in the rejection.

As to the explanation that the culture supernatant of Hideo et al comprises a polypeptide which comprises an amino acid sequence substantially identical to SEQ ID NO; 24 and inherently comprises the culture supernatant comprises 20% of the cell protein present in the composition, as set forth in the rejection above, said culture supernatant is prepared from *E. coli* EHEC O157:H7 under identical conditions as the instant specification (see example 1 and compare to preparation of cell culture supernatant to maximize the synthesis of cell culture supernatant proteins on p. 23 of Finlay et al) under which a protein comprising the sequence of SEQ ID NO: 24 or NleA (see annotation for SEQ ID NO: 24 in sequence listing) is produced. Therefore, the culture supernatant also comprises at least 20 % of the cell protein.

New Claim Rejections Based on Amendment to the claims

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 53-58, 71-72, 86 and 89-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hideo et al (JP20023550742A2, cited in IDS) in view of Li et al. US 2004/0180060 A1 9/16/2004 with priority to provisional application 60/454,183 filed March 12, 2003.

Hideo et al discloses a method of eliciting an immune response against E. coli O157:H7 comprising administering a effective amount of composition for inducing an immune response against E. coli O157:H7 comprising a protein specific to enterohemorrhagic E. coli O-157:H7 i.e. SEQ ID NO: 393 having at least 75%sequence identity to SEQ ID NO: 24 (see Appendix A for sequence alignment of SEQ ID NO: 24 with the protein of Hideo et al which includes abstract for the sequence annotation). See abstract, claim 4, claim 14, lines 1835-1840. Hideo et al also discloses treating an infection by E. coli O157:H7 using said composition. Hideo et al teach reducing the risk of O-157 infection or therapy of infection. See abstract and see line 1270, line 1945, paragraphs 51 and 53, paragraph 54 lines 9410-9415 and lines 9885-9890). treatment of the E. coli infection will result in reduction in colonization of E. coli in an animal and result in reduction in shedding of E. coli in an animal.

Hideo et al does not disclose practicing said method with a ruminant including bovines and ovines and does not disclose said composition further comprising an adjuvant.

Li et al teach that E. coli O157:H7 colonizes the intestines of ruminants and other animals and generally does not cause overt disease in these animals. Li et al teach that the shedding of the E. coli O157:H7 into feces of colonized animals serves as a source of E. coli infection in humans and it is important therefore to eradicate or reduce O157:H7 shedding in animals particularly cattle to prevent human infection. See paragraphs 3-5. Li et al teach adjuvanted vaccines comprising O157:H7 antigens for the reduction of O157:H7 colonization in animals or ruminants particularly cattle and methods of administering same to cattle to prevent shedding. See paragraphs 2, 8, 23.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to have practiced the method of Hideo et al in ruminants or cattle, thus resulting in the instant invention with a reasonable expectation of success. The motivation to do so is because Li et al teach that that the shedding of the E. coli o157:H7 into feces of colonized animals serves as a source of E. coli infection in humans and it is important therefore to eradicate or reduce O157:H7 shedding in animals particularly cattle to prevent human infection. Furthermore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the instant invention was made to have included an adjuvant in the composition for practicing said method in ruminants or cattle, as Li et at al teach that adjuvants

can be combined with O157:H7 antigens for the reduction of O157:H7 colonization in animals or ruminants particularly cattle and to prevent shedding. See paragraphs 2, 8, 23. Furthermore, the adjuvant of Li et al is beneficial as it helps to stimulate an immune response in the vaccinated ruminant.

Claim 88 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hideo et al (JP20023550742A2, cited in IDS) in view of Li et al. US 2004/0180060 A1 9/16/2004 with priority to provisional application 60/454,183 filed March 12, 2003 as applied to claims 53-58, 71-72, 86 and 89-95 above, further in view of in view of Finlay et al. WO 02/053181, cited in IDS.

The combination of Hideo et al and Li et al does not disclose that the composition further comprises EspA, EspB, EspD, EspC, intimin and Tir or further comprises an adjuvant.

Finlay et al teach a method for eliciting an immune response against E. coli EHEC O157:H7 or component thereof or a method for reducing colonization of an A/E pathogen or a method of reducing shedding (thus treating an infection by an A/E pathogen) in an animal comprising administering to the animal an effective amount of a composition comprising a culture supernatant (see p. 37-39 claims 1-26) wherein the composition comprises EspA, EspB, EspD, EspC, intimin and Tir (see p. 23 example 1 and figure 1 and p. 37claim 9) and/or further comprises an adjuvant (see p. 19 and p. 37 claims 4-8).Finlay et al teaches that said composition treats the EHEC infection and/or reduces colonization of the animal. See p. 2 under summary of the invention. Finlay et al teach that administration of said composition to an animal stimulates an immune response against one or more secreted antigens, such as EspA and Tir, which blocks attachment of the EHEC to intestinal epithelial cells.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to have combined the composition of Hideo et al and Li et al as combined with that of Finlay et al, thus resulting in the instant method (wherein the composition further comprises EspA, EspB, EspD, EspC, intimin and Tir or further comprises an adjuvant) with a reasonable expectation of success. The motivation to do so is because both compositions are individually taught in the prior art to be useful for the same purpose i.e. inducing an immune response against E. coli EHEC O157:H7 ("It is prima facie obvious to combine two

compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)) and Finlay et al provides additional motivation in that administration of said composition to a animal stimulates an immune response against one or more secreted antigens, such as EspA and Tir, that blocks attachment of the EHEC to intestinal epithelial cells.

Status of Claims

Claims 53-58, 71-73 and 86-95 are rejected. No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is (571)272-9939. The examiner can normally be reached on M-F 8:30 am- 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Oluwatosin Ogunbiyi/
Primary Examiner, Art Unit 1645